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Comparison of the effects of desflurane and total intravenous anesthesia on the optic nerve sheath diameter in robot assisted laparoscopic radical prostatectomy

A randomized controlled trial

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Abstract

Background: Optic nerve sheath diameter (ONSD) is a well-known surrogate marker for intracranial pressure during robot-assisted laparoscopic radical prostatectomies (RALP). ONSD during RALP is known to increase due to elevated intracranial pressure as a result of the steep Trendelenburg position and carbon dioxide pneumoperitoneum. We aimed to compare the effects of total intravenous anesthesia (TIVA) and desflurane anesthesia (DES) on ONSD during RALP.

Methods: Patients scheduled for RALP were enrolled and randomly assigned to the TIVA (propofol and remifentanil) or DES (desflurane and remifentanil) group in this randomized trial. Ultrasonographic measurements of ONSD were conducted before administration of anesthesia (T0), 10 minutes after the Trendelenburg position (T1), 1 hour after the Trendelenburg position (T2), 2 hours after the Trendelenburg position (T3), 10 minutes after resuming the supine position (T4), and at the time of arrival in the post-anaesthetic care unit (T5). The primary outcome measure was the mean ONSD at T2 of the TIVA and DES group during RALP.

Results: A total of 56 patients were analysed in this study. The mean ONSD at T1, T2, T3, and T4 were significantly lower for patients in the TIVA group compared with those in the DES group ($P = .023$, .000, .000, and .003, respectively).

Conclusion: The mean ONSD for patients in the TIVA group was significantly lower than that in the DES group during the RALP procedure. Our findings suggest that TIVA may be a more suitable anesthetic option for patients at risk of cerebral hypoperfusion.

Abbreviations: BIS = bispectral index score, CBF = cerebral blood flow, CSF = cerebrospinal fluid, DES = desflurane anesthesia, $ETCO_2$ = end-tidal CO_2, ICP = increase intracranial pressure, MAP = mean arterial pressure, ONSD = optic nerve sheath diameter, PONV = postoperative nausea and vomiting, RALP = robot-assisted laparoscopic radical prostatectomy, TCI = target-controlled infusion, TIVA = total intravenous anesthesia.

Keywords: intracranial pressure, optic nerve sheath diameter, robot-assisted laparoscopic radical prostatectomy, TIVA

1. Introduction

Robot-assisted laparoscopic radical prostatectomy (RALP) requires a steep Trendelenburg position and carbon dioxide pneumoperitoneum to optimise surgical exposure,[1] which could increase intracranial pressure (ICP) by up to 10 mmHg above baseline[2]. Previous studies have shown that measurement of optic nerve sheath diameter (ONSD) using ultrasonography is a non-invasive and reproducible technique for assessing elevated ICP.[3] Although it is known that ONSD increases during RALP according to the position and CO_2 insufflation, the effects of anesthetics on the change in ONSD have not been explored. Volatile anesthetics, which were used for RALP in previous studies,[2,4,5] increase ICP through vasodilation of vascular smooth muscle.[6,7] In contrast, total intravenous anesthesia (TIVA) with propofol has been shown to reduce cerebral blood flow (CBF) and thereby decrease ICP.[6,8]

We hypothesised that TIVA would reduce the increase in ONSD during RALP when compared to volatile anesthetics. The primary outcome measure was the mean ONSD at T2 (1 hour after the Trendelenburg position) of the TIVA and DES group, and the secondary outcome was the mean ONSD of the other time points, the change in mean arterial pressure (MAP) and end-tidal CO_2 ($ETCO_2$) during RALP.

2. Methods

After approval of this study was provided by the Institutional Review Board (June, 2016 for the Seoul National University Bundang Hospital, Seongnam, Korea), written informed consent

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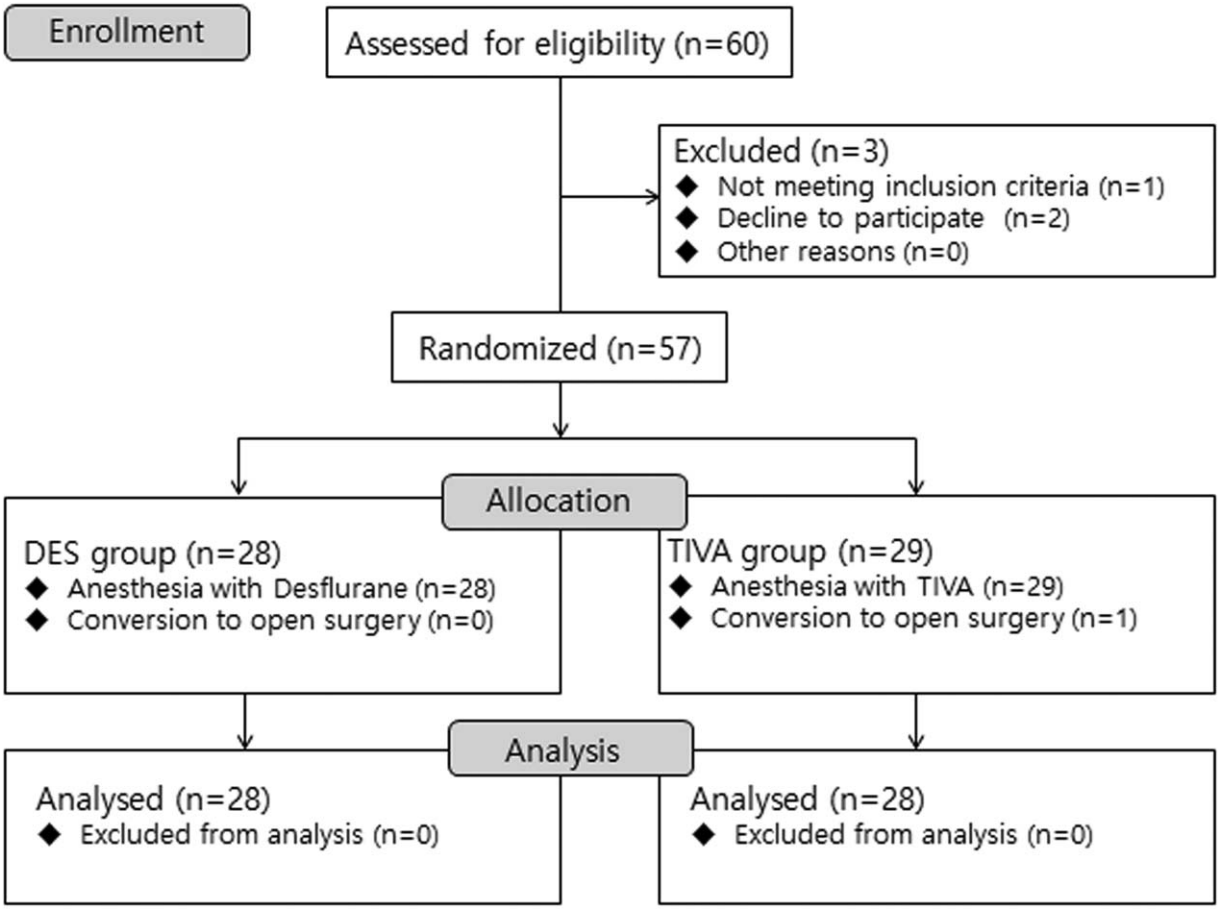

Figure 1. CONSORT flow diagram.

was obtained from all patients included in our study. The trial was registered with ClinicalTrials.gov (number NCT03152981). In total, 60 patients, aged 18 years or above and with an American Society of Anesthesiologists physical status of I or II, were enrolled in this study (Fig. 1). This prospective, randomised double-blinded trial was conducted in patients who received RALP using the da Vinci^{TM} robot system (Intuitive Surgical, Inc., Mountain View, CA) under general anesthesia. Exclusion criteria included pre-existing neurologic or ophthalmic disease or a history of neurosurgery or ophthalmic surgery.

2.1. Study protocol

A total of 60 patients were randomly assigned (in blocks of 4) to the desflurane anesthesia (DES) group or TIVA group by a computerised randomisation table. The interventions were sealed in sequentially numbered, opaque envelopes by the attending nurse not part of the project group. The sealed randomization envelopes were kept blinded for the patient and the staff until the day of the surgery and were opened by the attending nurse at the pre-operative holding area. After induction of anesthesia, the anesthetic vaporiser, and target-controlled infusion (TCI) pump were covered by surgical drapes, such that the observer of ONSD not participating in induction was blinded to the type of anesthesia administered.

All patients were pre-medicated intravenously with 0.03 mg/kg midazolam just before the operation and received standardised anesthetic management. Upon arrival in the operating room and before administration of anesthesia, electrocardiogram, heart rate, pulse oximetry, and non-invasive mean blood pressure were measured. General anesthesia was induced with 1.5 mg/kg propofol, 3 ng/mL remifentanil using TCI, and 0.6 mg/kg rocuronium. Following tracheal intubation, a radial artery catheter was inserted for continuous monitoring of blood pressure. Depth of anesthesia was monitored using a bispectral index score (BIS) monitor. Anesthesia was maintained between a BIS value of 40 to 60. In the DES group, anesthesia was maintained with desflurane and remifentanil. The end-tidal concentration of desflurane was maintained within the range of 4% and 7%, and the effect site concentrations of remifentanil between 2 to 3 ng/mL. In the TIVA group, anesthesia was maintained with propofol and remifentanil through TCI. The effect site concentrations of propofol and remifentanil were maintained within the range of 3 to 4 μg/mL for propofol and 2 to 3 ng/mL for remifentanil. If hypotension (< 20% of baseline systolic arterial pressure or MAP of < 25% of baseline values for > 5 min.) occurred, ephedrine 5 mg IV was used. Controlled ventilation was performed with O_2/air to maintain an end-tidal CO_2 ($ETCO_2$) of 30 to 35 mmHg during the surgery. CO_2 pneumoperitoneum was maintained with an intra-abdominal pressure of 15 ± 5 mmHg and a 40' Trendelenburg position.

Ultrasound measurements (VIVID I; GE Healthcare, Seoul, Korea) of ONSD were made with a 13 MHz linear ultrasound probe. Both eyelids were taped closed with Tegaderm films, and

ultrasound gel was applied over the closed left upper eyelid. ONSD was measured 3 mm behind the papilla in the left globe, perpendicular to the axis of the optic nerve, once in the transverse plane of each eye. The average of the 2 values measured in both eyes was calculated. A total of 6 measurements were performed at defined time points: before anesthesia administration (T0), 10 minutes after the Trendelenburg position (T1), 1 hour after the Trendelenburg position (T2), 2 hours after the Trendelenburg position (T3), 10 minutes after resuming the supine position (T4), and at arrival in the post-anesthetic care unit (T5). All scans of the optic nerve were performed by 1 experienced anesthesiologist, who had performed more than 30 scans. Subsequently, ONSD was determined using an electronic calliper. The primary outcome measure was the mean ONSD at T3 of the TIVA and DES group. Additional data, including body mass index, operation time, and anesthetic time, were collected for each patient. The MAP and $ETCO_2$ were recorded at 6 discrete time points. Intervention was discontinued when the robot-assisted prostatectomy was converted to the open surgery.

2.2. Statistical analysis

A previous study reported an ONSD of 5.5 ± 0.5 mm for RALP patients who received volatile anesthetics.[9] To detect a mean difference of 0.5 mm in ONSD between the groups, a sample size of 28 patients per group was required, with a type I error of 0.05 and a power of 90%, considering a 15% dropout rate.

All data were analysed using SPSS software (ver. 18.0; SPSS Inc., Chicago, IL). Continuous variables are presented as means ± standard deviation. Distribution of the data was analysed using the Shapiro-Wilk test. Non-normally distributed data were observed, nonparametric test was used for data analysis. The mean ONSD of the DES group and the TIVA group were analysed using the Student *t* test at each time point. Mann–Whitney *U* test was used in the 2 group comparison of the mean OSND not showing normal distribution. Dichotomous variables were analysed using chi-square or Fisher exact test. P value $< .05$ was considered statistically significant.

3. Results

We enrolled 60 patients to the study but dismissed 3 patients because 1 patient had an ophthalmic disease (glaucoma) and 2 patients declined to participate in the study. A total of 57 patients were assigned to 1 of the 2 groups (28 to DES group, 29 to TIVA group). Intervention in 1 patient in the TIVA group was discontinued because the robot-assisted prostatectomy was converted to the open surgery at 95 minutes after induction of anesthesia due to the errors in robot movements. A Total of 56 patients were analysed; there were 28 patients in each of the DES and TIVA groups (Fig. 1).

There were no significant differences in patient demographics, preoperative and intraoperative data associated with underlying diseases, anesthesia time, and operating time between the 2 groups (Table 1).

The mean values of ONSD at time points T1, T2, T3, and T4 during anesthesia were significantly increased compared to the ONSD values before anesthesia administration (T0). Our primary endpoint, the mean ONSD at T2, was lower for patients in the TIVA group compared with those in the DES group [5.28 ± 0.31 mmversus4.91 ± 0.21 mm,respectively;meandifference,0.36;95%CI,0.22to0.51;P = .000] (Table 2, Fig. 2). Furthermore mean ONSD at T1, T3, and T4 were significantly lower for patients in the TIVA group compared with those in the DES group (P = 0.023, 0.000, and 0.003, respectively). ONSD was restored to normal following recovery (Table 2, Fig. 2). MAP and $ETCO_2$ were comparable between the DES and TIVA groups (Table 3). Neurological complications were not observed in any of the patients during the perioperative period of RALP.

Table 1

Patient characteristics.

	DES group (n = 28)	TIVA group (n = 28)	*P*
Age, yr	66 ± 6	66 ± 8	.576
Height, cm	165 ± 7	166 ± 5	.794
Weight, kg	67 ± 6	67 ± 7	.846
Body mass index	24 ± 1	25 ± 3	.441
Diabetes mellitus	5 (18)	4 (14)	1.000
Hypertension	11 (39)	10 (36)	.783
Respiratory disease	1 (4)	2 (7)	.553
Operating time, min	173 ± 41	175 ± 27	.828
Anesthesia time, min	217 ± 43	217 ± 27	.985

Data area expressed as the mean ± SD or number of patients (%). DES = desflurane anesthesia, TIVA = total intravenous anesthesia.

Table 2

Comparison of the mean ONSD between 2 groups.

	DES group (n = 28)	TIVA group (n = 28)	Difference of the means	95% CI	*P*
ONSD (mm)					
Basal (T0)	4.44 ± 0.19	4.45 ± 0.17	-0.01	-0.14 to 0.05	.339*
T1	4.82 ± 0.29	4.66 ± 0.21	0.16	0.02 to 0.30	.023†
T2	5.28 ± 0.31	4.91 ± 0.21	0.36	0.22 to 0.51	.000†
T3	5.56 ± 0.37	5.15 ± 0.25	0.42	0.25 to 0.59	.000*
T4	5.12 ± 0.39	4.91 ± 0.22	0.26	0.09 to 0.43	.003†
T5	4.64 ± 0.24	4.61 ± 0.22	0.04	-0.09 to 0.16	.375*

Data area presented as the mean ± standard deviation. ONSD = optic nerve sheath diameter, CI = confidence interval, DES = desflurane anesthesia, TIVA = total intravenous anesthesia, T0 = before induction of anesthesia, T1 = 10 minutes after Trendelenburg position, T2 = 1 hour after Trendelenburg position, T3 = 2 hours after Trendelenburg position, T4 = 10 minutes after resuming supine position, T5 = arrival in the PACU.

* Mann–Whitney *U* test

† Student *t* test.

4. Discussion

Our study showed that the Trendelenburg position and CO_2 pneumoperitoneum in RALP increased the diameter of the optic nerve sheath in patients under anesthesia. The mean values of ONSD for patients in the TIVA group were significantly lower than that in the DES group. Despite the increase in ONSD, no neurological complications were observed.

ONSD during RALP increased as a result of the Trendelenburg position and CO_2 pneumoperitoneum. Previous studies have shown that the change in ONSD is associated with ICP changes.[3] The cerebrospinal fluid (CSF) in the dural sheath of the optic nerve is in contact with the CSF in the intracranial subarachnoid space. Hence, ICP is directly transmitted to the CSF in the optic nerve sheath. The subarachnoid space of the optic nerve sheath has an elastic trabecular anatomy and is most distensible 3 mm behind the papilla in the globe.[2] This distensibility allows the optic nerve sheath to inflate within a few minutes of exposure to elevated ICP. The Trendelenburg position alone has been shown to induce a moderate elevation in

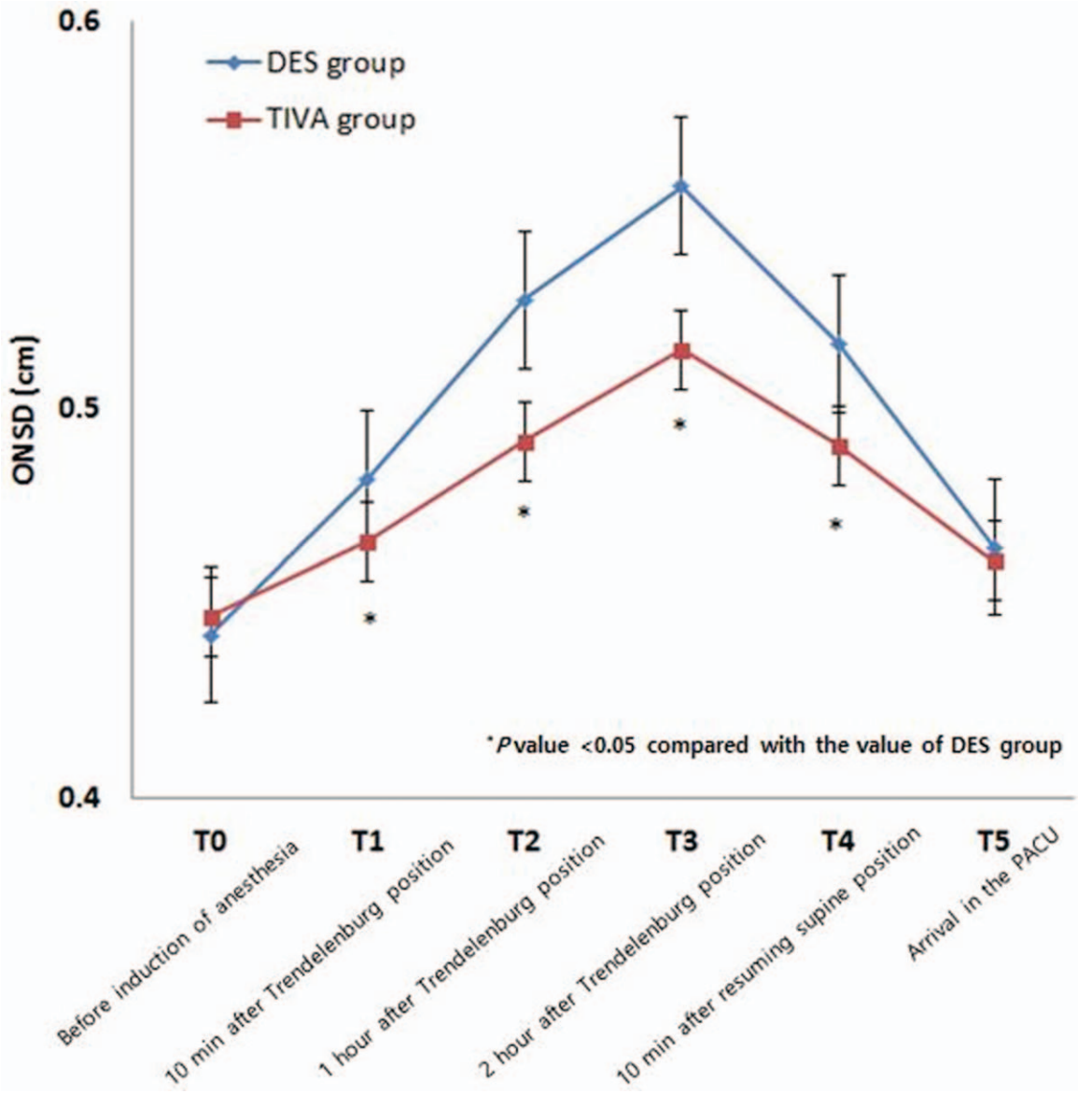

Figure 2. Changes in ONSD values between the 2 groups during RALP. Graph shows the mean values and standard deviations. ONSD = optic nerve sheath diameter, RALP = robot-assisted laparoscopic radical prostatectomy.

ICP (9–13 mmHg) with intracranial monitoring.[10] Increased intra-abdominal pressure due to CO_2 pneumoperitoneum has been shown to impair CSF drainage and increase ICP.[11] Collectively, these findings suggest that the Trendelenburg position and CO_2 pneumoperitoneum may increase ICP synergistically.

We observed significant differences in ONSD between the DES and TIVA groups. Propofol constricts cerebral vascular smooth muscle.[12] Elevation of cerebral vascular resistance appears to induce a reduction in CBF. A previous study showed that propofol decreased the cerebral metabolic rate (CMR) by 36%, and ICP by 30%, in patients with normal ICP.[13] Use of propofol for cerebral ischemia during neurosurgical operations is believed to confer a neuroprotective effect against mild ischemic insults.[14] Although perioperative neurologic complications following robotic surgery are rare, neurologic deterioration in the post-anesthetic care unit,[15] and vision changes with ischemic optic neuropathy,[16] have been reported. It is unlikely that increased ICP during RALP has clinical significance without intracranial pathology. Nonetheless, the neuroprotective properties of propofol may be beneficial to patients with ischemic cerebral disease.

In contrast to our results, Verdonck and colleagues showed that ONSD remained constant during the intraoperative period of RALP under sevoflurane anesthesia.[2] They observed a mean ONSD of approximately 5.0 mm. In previous studies and our study, the mean ONSD was shown to increase up to 5.5 mm under desflurane anesthesia. Although it is well known that desflurane causes greater increases in CBF than sevoflurane, it is unclear whether differences in the anaesthetic agents used caused these conflicting results. In the study of Verdonck and colleagues, the baseline ONSD was 5.0 mm and this was maintained throughout the surgery. However, other studies have reported a baseline ONSD of approximately 4.5 mm. Further studies are required to investigate these differences.

Table 3

Comparison of mean arterial pressure and end tidal CO_2 between 2 groups.

	DES group (n = 28)	TIVA group (n = 28)	P
Mean arterial pressure (mmHg)			
T0	69 ± 10	65 ± 6	.131
T1	95 ± 18	92 ± 12	.415
T2	78 ± 15	76 ± 13	.654
T3	71 ± 22	77 ± 9	.608
T4	79 ± 10	81 ± 12	.403
T5	88 ± 13	86 ± 13	.435
End tidal CO_2 (mmHg)			
T0	31 ± 2	30 ± 2	.307
T1	32 ± 3	32 ± 3	.962
T2	33 ± 4	33 ± 2	.965
T3	30 ± 11	34 ± 5	.783

Data area presented as the mean ± standard deviation. DES = desflurane, TIVA = total intravenous anesthesia, T0 = before induction of anesthesia, T1 = 10 minutes after Trendelenburg position, T2 = 1 hour after Trendelenburg position, T3 = 2 hours after Trendelenburg position, T4 = 10 minutes after resuming supine position, T5 = arrival in the PACU.

Postoperative nausea and vomiting (PONV) were not evaluated in this study. CO_2 pneumoperitoneum during laparoscopy leads to peritoneal stretching and irritation, which increase the risk of PONV.[17] Elevated ICP is also 1 of the risk factors for PONV.[18] Based on the results of this study, we can expect that TIVA will decrease the elevation of ICP compared to volatile agents and reduce the incidence of PONV in RALP. Additional study is required to elucidate the effects of increased intracranial pressure on PONV in RALP patients. It is well known that TIVA with propofol significantly decreases PONV compared to volatile anesthetics.[19] Moreover, TIVA with propofol is recommended for RALP patients to prevent PONV during the early postoperative period.[20]

Several limitations of this study should be noted. First, although the observer was blinded to the type of anesthesia, they were not blinded to the ONSD measurement time points. Thus, observer bias may be reflected in the ONSD measurements done at the specified time points during RALP. Second, the patients in our study did not have pre-existing intracranial pathology based on the exclusion criteria. Therefore, the effects on ICP in patients with intracranial pathology were not evaluated in this study. Patients with pre-existing elevated ICP or cerebral ischemia may experience different results in terms of ONSD.

In conclusion, the Trendelenburg position and CO_2 pneumoperitoneum during RALP increased the diameter of the optic nerve sheath. The mean ONSD in the TIVA group was significantly less than that in the DES group during the RALP operation. Our findings suggest that TIVA may be a more suitable choice for patients at risk of cerebral hypoperfusion, or with increased ICP.

Author contributions

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